UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/663,889	09/18/2000	Gary J. Nabel	8642/91	6450

757 7590 09/12/2002

BRINKS HOFER GILSON & LIONE
P.O. BOX 10395
CHICAGO, IL 60610

EXAMINER
PARAS JR, PETER

ART UNIT	PAPER NUMBER
1632	12

DATE MAILED: 09/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/663,889	NABEL ET AL.	
	Examiner	Art Unit	
	Peter Paras	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 17-54* is/are pending in the application.

4a) Of the above claim(s) *1 and 37-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *12* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's preliminary amendment filed on 9/19/01 has been entered. Claims 2-16 have been cancelled. New claims 17-54 have been added. Claims 1 and 17-54 are pending and are under current consideration.

Priority

This application repeats a substantial portion of prior Application Nos. 08/533,942, 09/031,572, and 09/426,325, filed 9/26/95, 2/26/98 and 10/25/99, respectively and adds and claims additional disclosure not presented in the prior application; the additional disclosure is **a kit**, which comprises a nucleic acid comprising a gene encoding p21 and a catheter. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Applicant's claim of priority to Application Nos. 08/533,942, 09/031,572, and 09/426,325, now US Patent Nos. 5,863,904, 6,057,300, 6,218,372 respectively, is denied. The parent applications fail to fulfill the requirements of 35 U.S.C 120 by not meeting the requirements of the first paragraph of 35 U.S.C. 112, particularly written description and new matter, necessary to support the claims of the instant application. See the MPEP at 201.11. In particular, the claim limitations as follows are not described in the instant specification: a kit comprising a catheter and a nucleic acid comprising a gene encoding p21. See the rejection under 35 U.S.C. 112, 1st paragraph, below.

Oath/Declaration

This application presents a claim for subject matter not originally claimed or embraced in the statement of the invention. The newly claimed subject matter is a kit comprising a catheter and a nucleic acid comprising a gene encoding p21. A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02. Also see the MPEP 602.05(a).

Sequence Compliance

Applicants sequence listing in paper and computer readable forms has been entered.

Election/Restrictions

As noted in the attached Interview Summary, claim 1 was inadvertently omitted from the original restriction requirement mailed on 12/26/01. A supplemental restriction requirement now including claim 1 is set forth below.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 17-36, drawn to a kit for site-specifically transforming cells *in vivo* comprising a catheter and a nucleic acid comprising a gene encoding p21, classified in class 435, subclass 455.

II. Claims 37-54, drawn to a kit for treating disease in a patient comprising a syringe and a nucleic acid comprising a gene encoding p21, classified in class 514, subclass 44.

III. Claim 1, drawn to a method of treating cancer comprising administering *in vivo* a therapeutically effective amount of a composition comprising an expression vector comprising a gene encoding p21 and a pharmaceutical carrier, classified in class 514, subclass 44.

Inventions I and II are distinct each from the other. Inventions are distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation, different functions, and different effects; the different inventions have different uses. Groups I and II comprise materially different products, namely a syringe and catheter, that result in different modes of operation and can be used in methods having different method steps that require materially different reagents and different technical considerations as the subject matter of both groups embraces different intended uses, such as site-specific transformation of cells *in vivo* and treating a disease in a patient. Because these inventions are distinct for the reasons given above and have acquired a

separate status in the art because of their recognized divergent subject matter and separate search requirement, restriction for examination purposes as indicated is proper.

Inventions I and III are distinct each from the other. Inventions are distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation, different functions, and different effects. For example, the kit of Group I requires a syringe while the method of Group III as claimed does not require a syringe for practice. Moreover, the method of Group III does not require the kit of Group I and the kit of Group I does not require the expression vector of Group III. Even more, the intended use of the kit of Group I is directed to site-specific transformation of cells *in vivo* while the method of Group III is directed to treating cancer. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and separate search requirement, restriction for examination purposes as indicated is proper.

Inventions II and III are distinct each from the other. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different modes of operation, different functions, and different effects. For example, the kit of Group II requires a catheter while the method of Group III as claimed does not require a catheter

for practice. Moreover, the method of Group III does not require the kit of Group II and the kit of Group II does not require the expression vector of Group III. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and separate search requirement, restriction for examination purposes as indicated is proper.

During a telephone conversation with John Murray on 9/5/02 a provisional election was made without traverse to prosecute the invention of Group I, claims 17-36; Applicants reaffirmed their election without traverse of the group I claims. See the election received on 3/20/02. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1 and 37-54 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112, 1st paragraph

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

Claim 17 (and dependent claims 18-36) are directed to **a kit comprising a catheter and a nucleic acid comprising a gene encoding p21**.

The specification provides no implicit or explicit support for a kit that comprises a catheter and a nucleic acid comprising a gene encoding p21 encompassed by the bolded text. The specification has only provided support for use of a catheter and an expression vector comprising a gene encoding p21 in a treatment method but has not otherwise even contemplated a kit comprising the same.

Claim 18 is directed to a kit comprising a catheter and a nucleic acid comprising a gene encoding p21, wherein **the catheter is a single-balloon catheter**. The specification provides no implicit or explicit support for a single-balloon catheter. The specification has only provided support for a double-balloon catheter.

Applicants are reminded that it is their burden to show where the specification supports any amendments to the claims. See 37 CFR 1.121 (b)(2)(iii), the MPEP 714.02, 3rd paragraph, last sentence and also the MPEP 2163.07, last sentence.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure.*

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21 and 32-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites the limitation "the pharmaceutical carrier" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 32 is indefinite as written. The claim is indefinite because the term genetic therapeutic has not been defined by the specification. It is unclear what is meant or encompassed by the term. Further, the term genetic therapeutic does not appear to be an art-recognized term used to define a particular class of proteins as it would appear that a "genetic therapeutic" is a protein product encoded by the second gene. As such the claim is indefinite as written.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17 and 19-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Nabel et al (US 5,863,904).

The claims are directed to a kit comprising a catheter and a nucleic acid comprising a gene encoding p21. For the purposes of this rejection the limitation "kit" is not given patentable weight, as it is an intended use for its components.

Nabel et al teach the administration of an adenoviral vector comprising a gene encoding p21 via a double-balloon catheter to the iliofemoral artery of a pig. See column 6, lines 22-58. Nabel et al also teach that the expression vector may be combined with a pharmaceutical carrier. See column 4, lines 31-33. Nabel et al further teach that the gene encoding p21 can be inserted into viral vectors, such as adenoviral

and retroviral vectors (see column 2 beginning on line 57 and bridging to column 3, line 22), wherein the viral vector may be incorporation into an acceptable formulation provided the viral particles are inactivated (see column 4, lines 37-50). Nabel et al teach that certain viral promoters, such as the CMV and RSV promoters may be inserted into an expression vector to drive expression of the p21 gene. See column 3 at lines 2-4. Nabel et al teach that such an expression vector containing a gene encoding p21 can be incorporated into a liposome and then delivered to a specific tissue. See column 4, lines 25-30. Finally Nabel et al teach that p21 can be expressed as a fusion protein, wherein the gene encoding p21 is fused to a second gene encoding an immunotherapeutic agent, genetic therapeutic agent, cytokine, or a prodrug converting enzyme, particularly thymidine kinase. See column 3 lines 53-60.

Thus, the teachings of Nabel anticipate all of the instant claim limitations.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *in re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 17 and 19-36 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,863,904. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims encompass a catheter and a nucleic acid comprising a p21 gene, wherein the nucleic acid comprising the p21 gene may be inserted into a pharmaceutical carrier, such as a liposome or inserted into a viral vector (which can be inserted into a viral particle, see column 4, lines 37-50) such as an adenoviral vector or a retroviral vector (US 5,863,904 has contemplated that a viral vector may be a retroviral vector, see column 2 beginning on line 57 and bridging to column 3, line 22, and has further contemplated that regulatory sequences driving the expression of the p21 gene may be viral promoters, such as CMV or RSV), and wherein the nucleic acid may comprise a second gene that is fused to the p21 gene to make a fusion gene, particularly a p21-thymidine kinase fusion gene.

Claims 17, 19-36 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,218,372 in view of US 5,863,904.

The claims of the instant application encompass a catheter and a nucleic acid comprising a gene encoding p21. The claims of US 6,218,372 encompass treatment of restenosis by direction introduction of a composition comprising an expression vector comprising a gene, which encodes p21. US 5,863,904 teaches that restenosis can be

treated by direct introduction of a nucleic acid comprising a gene encoding p21 to the site of restenosis via a catheter. See column 6, lines 22-58. As such, in light of the teachings of US 5,863,904 it would have been obvious to use a catheter to introduce a nucleic acid sequence, particularly a gene encoding p21, to the site of restenosis. Furthermore, the claims of US 6,218,372 and the claims of the instant application are not patentably distinct from each other because both sets of claims encompass a insertion of the nucleic acid encoding p21 into an expression vector, particularly a viral vector (the specification of US 6,218,372 contemplates that a suitable viral vector may be an adenoviral vector or a retroviral vector see column 2 beginning on line 63 and bridging to column 3, line 21, and has further contemplated that regulatory sequences driving the expression of the p21 gene may be viral promoters, such as CMV or RSV). Furthermore, both sets of claims encompass delivery of the nucleic acid via a virus particle, which can be interpreted to be a pharmaceutical carrier (in particular see claims 10 and 15 of US 6,218,372, which recite the concentration of viral particles to be introduced to the site of restenosis, also see the specification of US 6,218,372 at column 4, lines 37-55). US 5,863,904 also teach that other acceptable pharmaceutical carriers may be liposomes. Both sets of claims further encompass a second gene contained within the nucleic acid comprising the p21 gene. The second gene and the p21 gene in this context form a fusion gene, particularly a thymidine kinase-p21 fusion gene.

Claims 17 and 19-30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,057,300 in view of US 5,863,904.

The claims of the instant application encompass a catheter and a nucleic acid comprising a gene encoding p21. The claims of US 6,057,300 encompass treatment of restenosis by direction introduction of a composition comprising an expression vector comprising a gene, which encodes p21. US 5,863,904 teaches that restenosis can be treated by direct introduction of a nucleic acid comprising a gene encoding p21 to the site of restenosis via a catheter. See column 6, lines 22-58. As such, in light of the teachings of US 5,863,904 it would have been obvious to use a catheter to introduce a nucleic acid sequence, particularly a gene encoding p21, to the site of restenosis. Furthermore, the claims of US 6,057,300 and the claims of the instant application are not patentably distinct from each other because both sets of claims encompass a insertion of the nucleic acid encoding p21 into an expression vector, particularly a viral vector (the specification of US 6,057,300 contemplates that a suitable viral vector may be an adenoviral vector or a retroviral vector see column 2 beginning on line 57 and bridging to column 3, line 21, and has further contemplated that regulatory sequences driving the expression of the p21 gene may be viral promoters, such as CMV or RSV). US 5,863,904 also teaches that an expression vector comprising a nucleic acid comprising a p21 gene may be inserted into a pharmaceutical carrier for delivery to the site of restenosis, wherein the pharmaceutical carrier may be a liposome or a virus particle. See column 4, lines 31-50. The claims of US 6,057,300 when taken in light of

the teachings of US 5,863,904 make obvious to use a liposome or a virus to particle as a carrier for delivering the nucleic acid comprising the p21 gene.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Patsy Zimmerman whose telephone number is (703) 308-0009.

Peter Paras, Jr.
Art Unit 1632